Dear Ms. Kate-Louise Gottfried,

I respectfully offer the following comments on the Draft Interim Guidance on Financial Relationships :

General Comments

Not unexpectedly, the guidance document focuses primarily on the notion of "managing" financial conflicts of interest. I endorse the sentiments expressed by Dr. Marcia Angell at the Human Subject Protection and Financial Conflicts of Interest Conference held at the HIH in August 2000, directed at the notion of extirpating situations from which such conflicts arise. I specifically endorse the following recommendations:

* investigators who receive grant support from industry should have no other financial ties to those companies

* technology transfer does not require that fees be paid directly to investigators. Income from limited consulting might instead go to a pool earmarked to support the missions of the institution

* institutions and the (sic) senior officials should not have investments in any health care industry

[http://ohrp.osophs.dhhs.gov/coi/8-16.htm#Angell]

Specific comments

Clinical Investigators

2.2 "Any agreements between Investigators and a sponsor should be reviewed by the Institution's Conflict of Interest Committee or equivalent body."

Most IRBs do not function within institutions that have such a Committee. Many IRBs do not function within an institutional setting at all. The notion of such an institutional committee reviewing financial interests in lieu of the IRB is startlingly dissonant with the notion expressed in this statement in the guidance document: "Broad participation of members from outside the institution, who will have no interest in the outcome of the research or the business interests of the institution, is considered to be one of the most effective means of protecting the integrity of the IRB process."

Such Institutional Conflict of Interest Committees do not have non-institutional members, and the substance of their deliberations is not typically disclosed to the IRB membership. The IRB should not delegate its responsibility for evaluating potential financial conflicts of interest by acquiesing in such "substituted judgment."

The IRB should determine the presence of conflicting financial interests by collecting relevant information from investigators in the context of Applications for Research (initial review), and should ensure compliance with institutional policies concerning such interests. The presence of non-affiliated community members on the IRB is important in this respect. I note here the recommendation concerning such membership by the NBAC in its draft report on Ethical and Policy Issues in Research Involving Human Participants:

Recommendation 4.8: The National Office of Human Research Oversight (NOHRO) should issue new regulations setting minimum percentage requirements for IRB membership composition and quorum determination for members who 1) are not otherwise affiliated with the institution and 2) whose primary concerns are in non-scientific areas. At least fifty percent of the IRB members should be otherwise not affiliated with the institution and at least 50 percent of the IRB members should be non-scientists.

[http://bioethics.gov/human/chapt4.html]

Institutional policy should also mandate the reporting to the IRB of any changes in financial relationships or interests involving investigators that develop during the periods between "continuing reviews" performed by the IRB. Such changes should be considered the equivalent of "protocol amendments," the latter necessitating IRB review and approval and, when necessary, disclosure to current research subjects and modification of applicable Consent Documents.

5. Consent

"5.2 IRBs should take steps to ensure that the potential research participants are apprised of the source of funding for the study and the payment arrangements for Investigators during the consent process and in the Consent Form, whenever that information is considered to be material to the potential subjects' decision-making process."

The notion that certain information may be "material" without further clarification or discussion is unhelpfully ambiguous. I suggest that the source, mechanism and amount of payments made to investigators be disclosed routinely in the Consent Document. I refer you directly to comments I made concerning this during the aforementioned Financial Conflicts of Interest Conference :

http://ohrp.osophs.dhhs.gov/coi/cmann.pdf

I appreciate the opportunity to comment on your draft guidance.

Sincerely,

Howard Mann, M.D.
Chairman
Human Subjects and Research Committee
Intermountain Health Care
Salt Lake City